AMENDMENTS TO THE SPECIFICATION

Please replace Paragraph [00018] with the following replacement paragraph.

[00018] Figure 3 illustrates DNA sequences of the RASSF1A promoter that became methylated in siRNA transfected cells. The sequences shown in this figure are identical for each of pcDNA, siRASSF1Amut, siRASSF1Aprom, siRASSF1Atx and Melanoma and are set forth in SEQ ID NO:1.

Please replace Paragraph [00051] with the following replacement paragraph.

[00051] This example demonstrates expression of short hairpin RNAs that are complementary to regions of a human tumor suppressor gene RASSF1A. The consequences of this expression were monitored by determining the patterns of DNA methylation in the promoter and part of the coding region of this gene, which is also susceptible to methylation in cancer cells. The DNA sequence of the RASSF1A gene is depicted below:

RASSF1A Promoter (SEQ ID NO:2):

ggggctctgc gagagcgcgc ccagccccgc cttcgggccc cacagtccct gcacccaggt
ttccattgcg cggctctcct cagctccttc ccgccgccca gtctggatcc tgggggaggc
gctgaagtcg gggcccgccc tgtggccccg cccggcccgc gcttgct***agc*** gcccaaagcc

RASSF1A transcript (SEQ ID NO:3):

agcgaagcac gggcccaaCC GGgccatgtc ggggggagcct gagctcattg agctgcggga
gctggcaccc gctgggcgcg ctgggaaggg ccgcacccgg ctggagcgtg ccaacgcgct
gcgcatcgcg cggggcaccg cgtgcaaccc cacacggcag ctggtccctg gccgtggcca
ccgcttccag cccgcggggc ccgccacgca cacgtggtgc gacctctgtg gcgacttcat
ctggggcgtc gtgcgcaaag gcctgcagtg cgcgcgtgag tagtggcccc gcgcgcctac

agc is where transcription probably starts

atg is the methionine codon

The bolded sequences were targeted by siRNAs of the invention.

Please replace paragraph [00052] with the following replacement paragraph.

[00052] PCR reactions are performed using a plasmid containing the human U6 promoter as template to yield U6 transcription cassettes expressing siRNAs. The 5' oligonucleotide (5'U6 universal primer) is complementary to 29 nucleotides at the 5' end of the U6 promoter (bold italics indicate the nucleotides complementary to those on the promoter).

5'U6 Mlu primer:

5' AATCGA ACGCGT ***GGATCCAAGGTCGGGCAGGAAGAGGGCCT*** 3' (SEQ ID NO:4)
Mlu I U6

This U6 common 5' primer, used for all PCR steps, binds to the 5' end of the U6 promoter and includes an Mlu I restriction site for cloning purposes. The 3' oligonucleotides, which contain either the sense, antisense, or both siRNA-coding sequences (siDNAs), are depicted in Fig. 1 and described herein. The last 20 nucleotides at the 3' end of all 3' PCR primers are complementary to the last 20 nucleotides of the U6 promoter which is: 5'**GTGGAAAGG ACGAAACACCG3'** (SEQ ID NO:5). All PCR reactions were carried out as follows: 1 min. at 94°C, 1 min. at 55°C and 1 min. at 72°C for 30 cycles. The PCR products can be directly transfected into cells (e.g., with prior cloning into an expression vector), in which event the PCR primers can be kinased with non-radioactive ATP prior to amplification and purified on Quiagen columns prior to using them in the PCR reactions. The PCR products also can be purified on Quiagen columns.

The 3' primers used to make siRNA expression cassettes are depicted below:

Primers used to make PCR products encoding siRNA's complementary to the promoter region of the RASSF1A gene:

3'PR 1 (SEQ ID NO:6)

```
5'CTACACAAA GGCGGGCCCCGACTTCAGCG C   GGTGTTTCGTCCTTTCCACAA 3'
    loop          si-sense        +1          U6
```

3'PR 2 (SEQ ID NO:7)

```
5'AACTC GAATTC AAAAAA GCGCTGAAGTCGGGGCCCGCC  CTACACAAA 3'
       EcoRI   Ter.     si-antisense          Loop
```

Primers used to make PCR products encoding siRNA's complementary to the transcribed region of the RASSF1A gene:

3'TR 1 (SEQ ID NO:8)

```
5'CTACACAAA CGACATGGCCCGGTTGGGCC C    GGTGTTTCGTCCTTTCCACAA 3'
   loop          si-sense        +1          U6
```

3'TR 2 (SEQ ID NO:9)

```
5'AACTC GAATTC AAAAAA GGGCCCAACCGGGCCATGTCG   CTACACAAA 3'
       EcoRI Ter.        si-antisense          Loop
```

Please replace paragraph [00058] with the following replacement paragraph.

[00058] Figure 2 shows results of the MSP analysis of the RASSF1A promoter in siRNA transfected cells. In the figure, H_2O represents a water control used in the PCR reactions. The following additional abbreviations were also used:

pcDNA: Cells transfected only with the vector (no siRNA)

siRASSF1Amut: Cells transfected with the mutant siRNA vector

siRASSF1Aprom: Cells transfected with the siRNA vector directed against the RASSF1A promoter sequences

siRASSF1Atx: Cells transfected with the siRNA vector directed against the RASSF1A transcript

Melanoma: a control for RASSF1A methylation. This is DNA from a melanoma tumor, which is methylated in the RASSF1A promoter.

M, size markers

m, MSP done with primers specific for a methylated RASSF1A promoter

u, MSP done with primers specific for an unmethylated RASSF1A promoter

The following primers were used in the MSP reaction: methylated DNA-specific primers, M210 (5' GGGTTTTGCGAGAGCGCG 3') (SEQ ID NO:10) and M211 (5'GCTAACAAACGC GAACCG 3') (SEQ ID NO:11) or unmethylated DNA-specific primers UM240 (5' GGGGTTTTGT GAGAGTGTGTTTAG 3') (SEQ ID NO:12) and UM241 (5' TAAACACTAACAAACACAAAC CAAAC 3') (SEQ ID NO:13) (Liu, L. et al., 2002).

Please replace paragraph [00062] with the following replacement paragraph.

[00062] As a negative control, DNA was extracted from cells expressing a mutated siRNA, was analyzed, and showed no effects on the methylation of the RASSF1A gene. In this analysis, PCR products were produced as described in Example 1, but using the 3' primers shown below. For the mutant there were two transversions (CCGG to GGCC) and one transition (C to T) to make sure it would be inactive.

Mutant primers against transcribed region:

3'MT 1 (SEQ ID NO:14)

```
                (c)    (ccgg)
5'CTACACAAA CGATATGGCGGCCTTGGGCC C    GGTGTTTCGTCCTTTCCACAA 3'
     loop          si-sense        +1          U6
```

3'MT 2 (SEQ ID NO:15)

```
5'AACTC GAATTC AAAAAA GGGCCCAAGGCCGCCATATCG    CTACACAAA 3'
        EcoRI   Ter.       si-antisense         Loop
```